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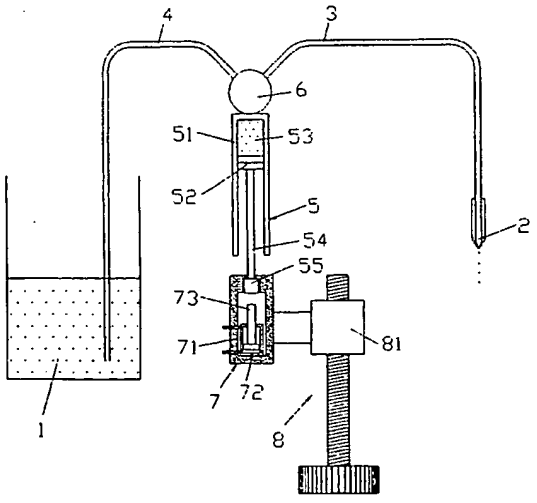
(54) Title: LOW VOLUME DROPLET DISPENSING



(57) Abstract: A low volume dispensing apparatus has a droplet dispensing assembly (5) having a cylinder (51) for containing a fluid to be dispensed and having a nozzle (2) at one end. Extending through the other end is a piston (52, 54). A driving device (8) is connected to the piston and cylinder to move the piston relatively outwardly or inwardly along the cylinder to draw fluid into the cylinder through the nozzle or to provide fluid to the nozzle for dispensing therefrom. An impulse driver (7) connected to the droplet dispensing assembly or to the driving device to dispense fluid from the cylinder through the nozzle in a pulsed manner. A sensor (102) may be used to sense the position of the dispensing apparatus relative to the individual wells (100) in a sample plate (104) into which liquid is to be dispensed.

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dispensing by the impulse driver respectively. The driving device may be connected to the supply channel to supply fluid to the cylinder in use.

A valve may be disposed between the nozzle and the piston, movable between a first position in which the supply channel is in communication with that part of the cylinder between the valve and the piston and a second position in which the supply channel is closed and that part of the cylinder between the valve and the piston is in communication with the nozzle. Preferably a fluid reservoir is connected to the supply channel.

The impulse driver may comprise a piezoelectric actuator, a pneumatic actuator, a solenoid actuator or the like.

The driving device may include a screw-thread drive or other step-less drive.

A seal is preferably provided between the piston and the cylinder.

The apparatus may include a plurality of droplet dispensing assemblies, wherein the cylinders of the dispensing apparatus are connected to a common manifold for fluid to be dispensed and the pistons extend through the manifold. The manifold may be connected to a supply line which is selectively engageable with the manifold.

According to a further aspect of the invention there is provided a low volume dispensing apparatus including

a droplet dispensing assembly arranged to be moved transversely across a sample plate having a plurality of wells or micro-tubes and to dispense droplets of liquid into the wells or micro-tubes;

a sensor positioned adjacent the droplet dispensing assembly and arranged to sense the location of the wells or micro-tubes or the dividing walls or the like therebetween and to provide a trigger signal indicative thereof; and

a circuit for actuating dispensing by the droplet dispensing assembly on receipt of the trigger signal.

Examples of devices constructed in accordance with the present invention will now be described with reference to the accompanying drawings in which:-

Figure 1 illustrates, diagrammatically, a first example of a dispensing apparatus;

Figure 2 illustrates stages in the operation of the first example;

Figure 3 illustrates a second example;

Figure 4 illustrates a modified version of the second example;

Figure 5 illustrates another modified version of the second example;

Figure 6 illustrates a further modified version of the second example;

Figures 7A and 7B illustrate stages in the operation of the modified example;

seat 75 and the piston rod head 55 being accurately controlled by the screw-thread drive 8 (Figure 2B).

To cause the dispensing of a precisely controlled amount liquid from the pipetting nozzle 2, the drive rod 73 is moved rapidly upwards between the position shown in Figure 2B and the position shown in Figure 2C, to drive the piston rod 54 upwards, until the piston rod head 55 re-engages the seat 75 and in so doing, as will be appreciated by referring to Figure 1, moving the piston 52 upwards and driving liquid from the liquid volume 53, through the three way valve 6 and the tube 3 and out of the end of the pipetting nozzle 2. The impulse drive piston 72 is then retracted to the start position as is shown in Figure 2D and the screw-thread drive 8 then moves the support 81 upwards, effectively lowering the piston rod head 55 inside the impulse drive unit 7, to allow another dispense cycle to be initiated.

It will be appreciated that a combination of the screw drive 8, which, in effect, provides a driving device to control the amount of liquid in the liquid volume 53 by either drawing it in to the volume 53 from the reservoir 1 or else (if desired) moving it back to the reservoir 1, and by using it to fix the distance of travel of the piston rod 54, very accurate control of the amount of liquid dispensed can be achieved.

Figure 3 illustrates a second example in which liquid to be dispensed is drawn directly into a pipetting nozzle or needle 2 by dipping the needle 2 into the liquid. In this example, the pipetting nozzle 2 has a cylindrical wall 21 which contains, as a close fit a piston 22. The piston may carry a piston seal (not shown) or else a seal may be provided at the top end (as shown in the figure) of the cylindrical wall 21, engaging the side of a piston rod 23 which is connected to the piston 22. At the opposite end of the piston rod 23 a piston rod head 24 is located within an impulse drive unit 7 which is substantially the same as that shown in Figures 1 and 2 and which operates in a substantially identical fashion and which is again carried by a screw-threaded drive 8.

In a modification of the Figure 3 example, shown in Figure 4, the impulse drive unit of Figure 3 is replaced with a impulse drive unit 7 which includes a piezoelectric actuator 76 having a head 24 which is connected to the piston rod 23, the actuator 76 being biassed by a coil spring 77 away from the seat 75. Actuation of the piezoelectric actuator 76 drives the piston 22 to dispense a droplet as before. The coil spring 77 maintains the actuator 76 in contact with the piston rod head 24.

In a further modification of the Figure 4 example, shown in Figure 5, the piezoelectric actuator 76 is directly connected to the head 24 of the piston rod 23.

In a further modification of the Figure 3 example, shown in Figure 6, fluid is supplied to the pipetting nozzle 2 via a supply conduit 90 connected to a port 91of the

into the manifold 9 and hence into the pipetting nozzles 2 and thereafter the pistons 22, 23 are inserted through the tops of the pipetting nozzles 2 by the action of the screw-thread drive 8. The impulse drive unit 7 can then be operated as before, in order to cause predefined amounts of liquid to be dispensed from the plural pipetting nozzles either for dispensing of a liquid reagent or for washing purposes as illustrated in Figure 9B.

Figure 10 illustrates a still further example, similar to that of Figure 8, but in which, instead of impacting the piston 22 within each pipetting nozzle 22 the pipetting nozzles are mounted on a carriage 27 which is supported against the bias of a spring 28 within a support 29 and the impulse drive unit 27 plural pistons 72 and cylinders 71 with associated drive rods 73 which are caused to impact against the carriage 27 to cause liquid to be dispensed through the pipetting nozzles 2.

Figure 11 illustrates a further modification of the example shown in Figure 3, in which, additionally, an optical (eg infra-red) sensor 102 is used to locate the position of dividing walls 101, which separate individual wells 100 in a sample plate 104 into which liquid is to be dispensed from the pipetting nozzle 2 of the apparatus as the nozzle 2 is moved over the wells 100, and to provide a trigger signal to a circuit 103 to actuate the impulse driver 7 to cause a droplet to be dispensed into the adjacent well 100. This is useful to overcome the tolerances or variations which occur in the size and spacing of the wells 100 (or micro-tubes) in a typical micro-titre sample plate, by sensing the positions of the dividing walls or the like and relating this to the position of the nozzle 2 to trigger dispensing into the adjacent well 100, rather than relying on the spacing between wells being absolutely uniform and advancing the nozzle across the sample plate in a series of fixed steps at each of which a droplet is dispensed.

A similar sensor may be used in connection with any of the examples shown above.

wherein the driving device is connected to the supply channel to supply fluid to the cylinder in use.

8. Apparatus according to any of claims 1 to 7, further including a valve disposed between the nozzle and the piston, and movable between a first position in which the supply channel is in communication with that part of the cylinder between the valve and the piston and a second position in which the supply channel is closed and that part of the cylinder between the valve and the piston is in communication with the nozzle.

9. Apparatus according to claim 6, or to claim 7 or claim 8 when dependent on claim 6, further including a fluid reservoir connected to the supply channel.

10. Apparatus according to any of claims 1 to 9, wherein the impulse driver comprises a piezoelectric actuator.

11. Apparatus according to any of claims 1 to 9, wherein the impulse driver comprises a pneumatic actuator.

12. Apparatus according to any of claims 1 to 9, wherein the impulse driver comprises a solenoid actuator.

13. Apparatus according to any of claims 1 to 12, wherein the driving device includes a screw-thread drive.

14. Apparatus according to any of claims 1 to 13, further including a seal between the piston and the cylinder.

15. Apparatus according to any of claims 1 to 14, having a plurality of droplet dispensing assemblies, wherein the cylinders of the dispensing apparatus are connected to a common manifold for fluid to be dispensed and the pistons extend through the manifold.

16. Apparatus according to claim 15, wherein the manifold is connected to a supply line.

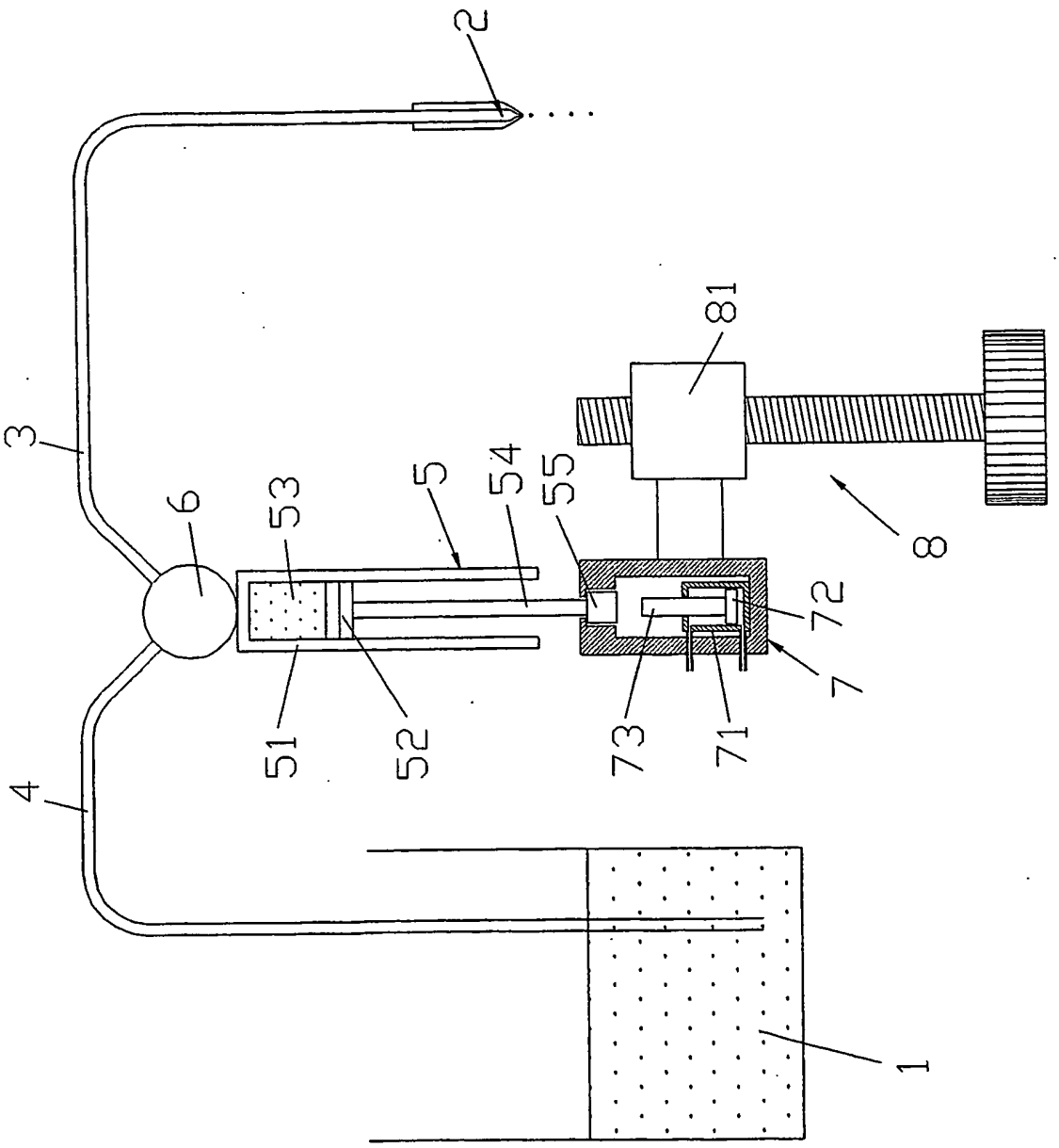

Fig 1

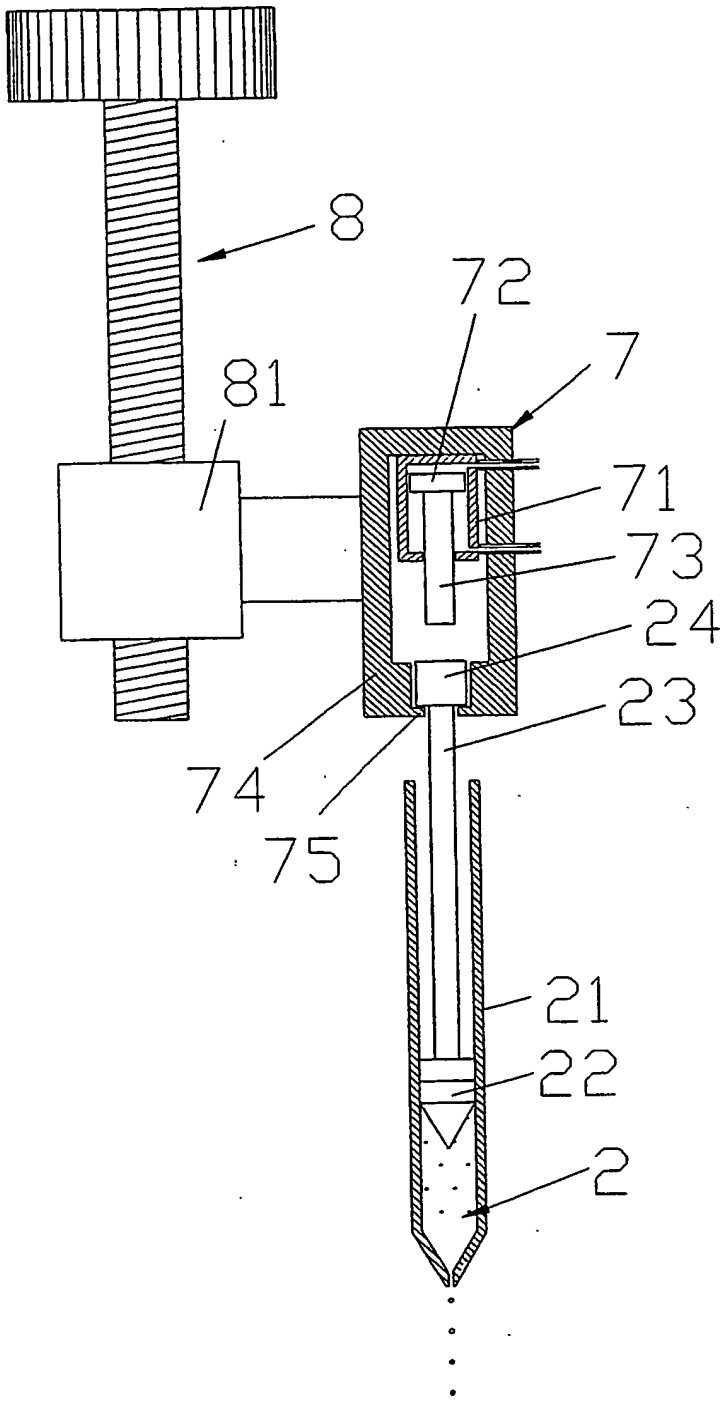

Fig 3

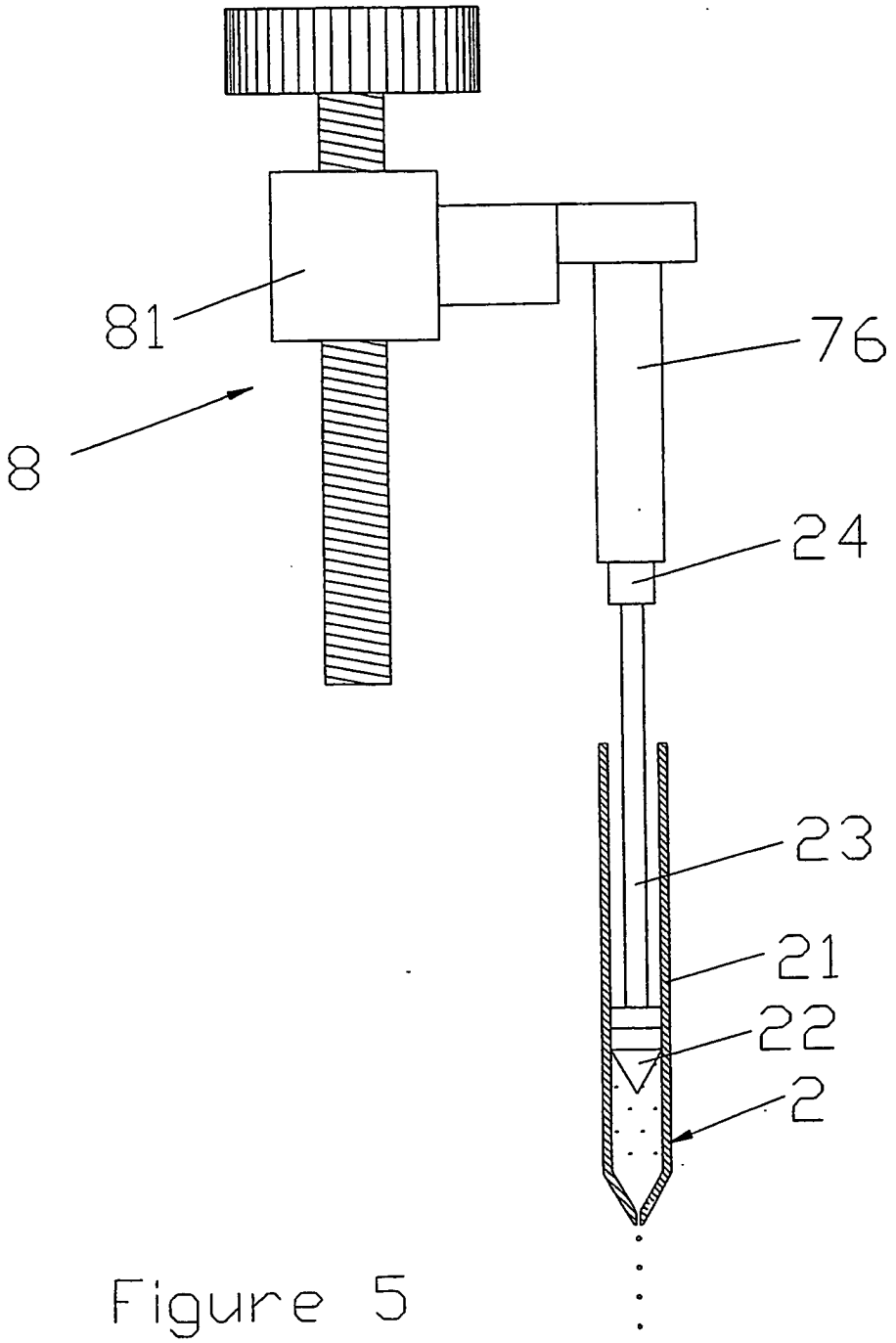

Figure 5

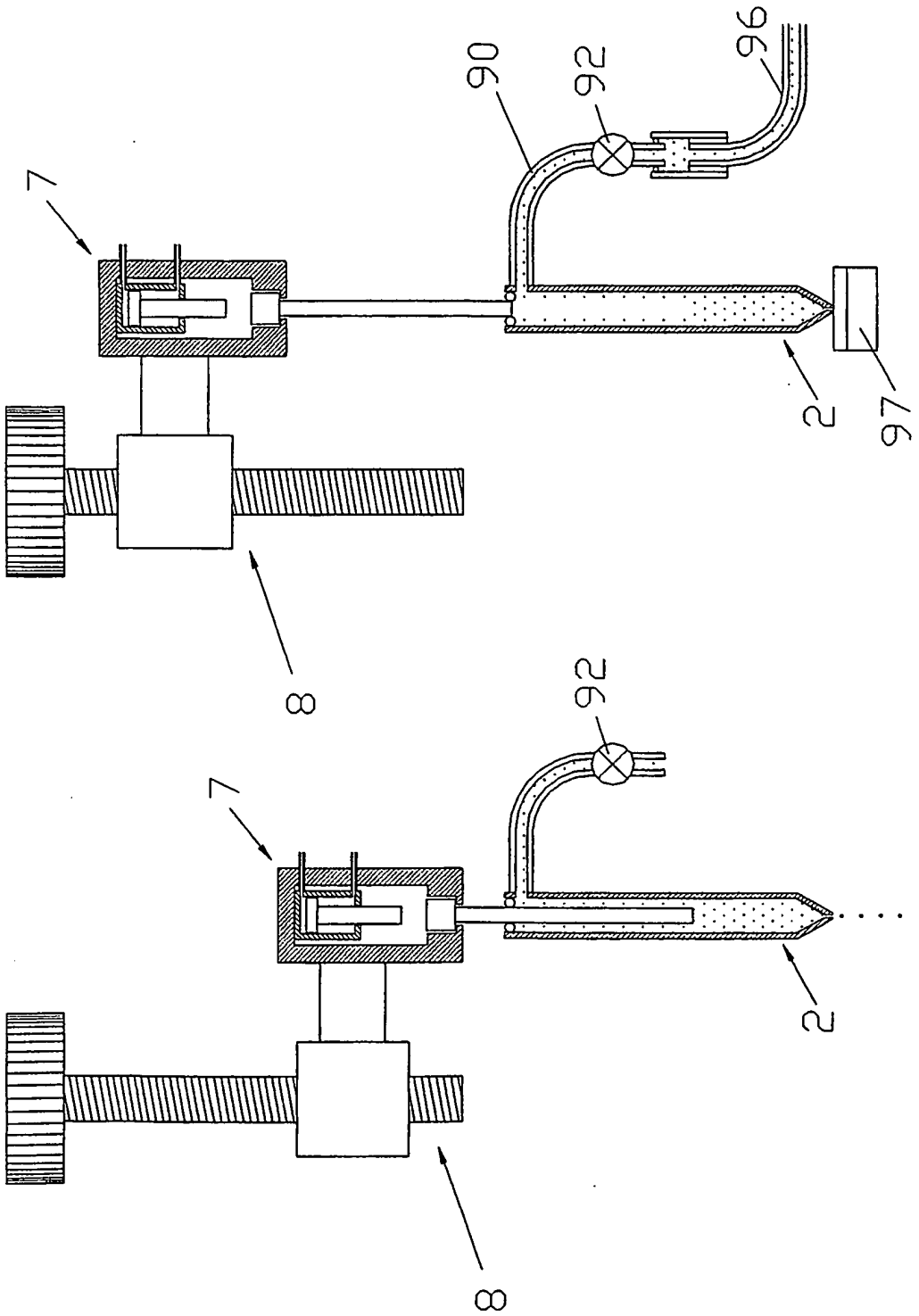

Figure 7B

Figure 7A

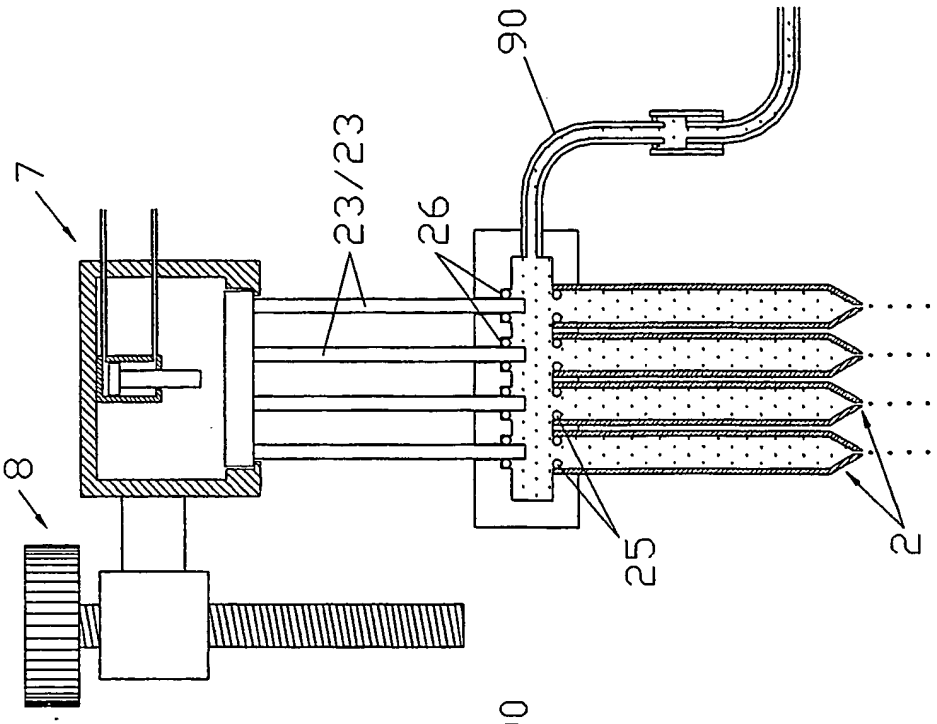

Figure 9B

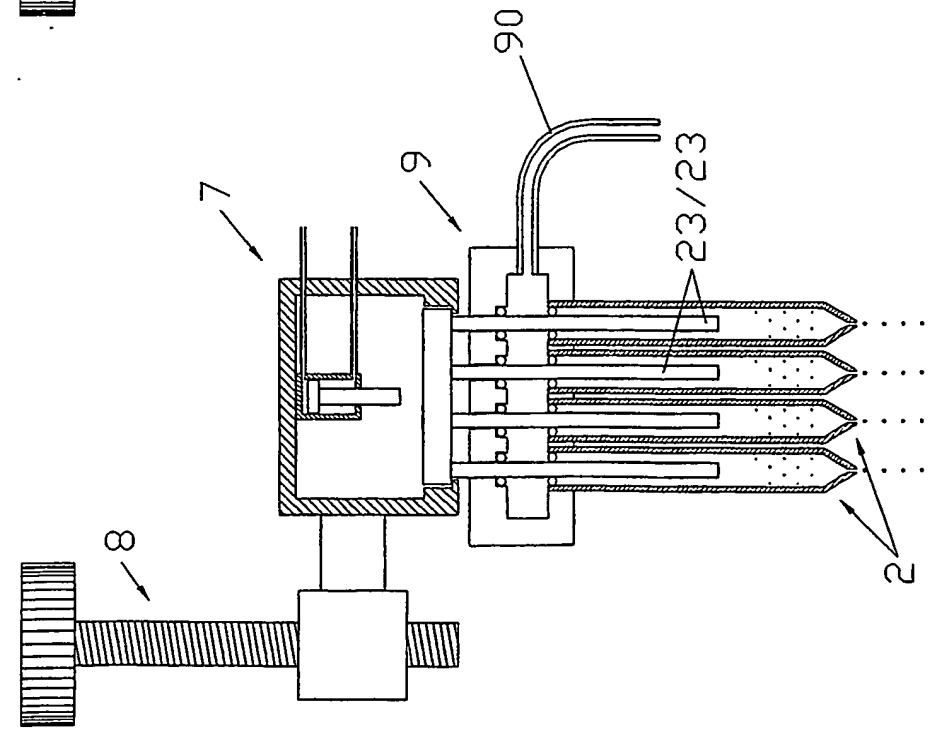

Figure 9A

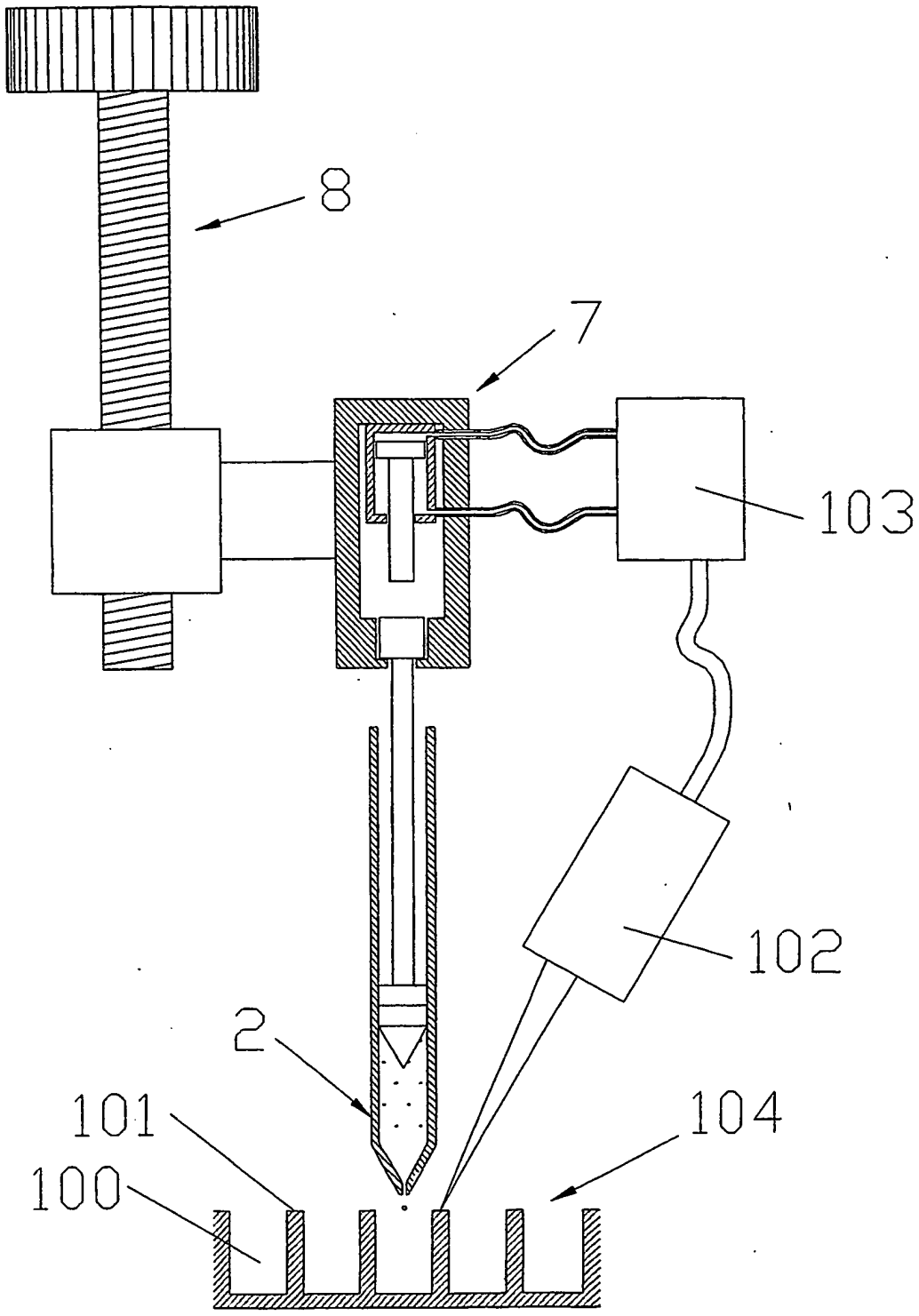

Figure 11

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/00431

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